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B1 cont

Committee of the International Union of Biochemistry and Molecular Biology (IUBMB) (see, for example, www.expasy.ch/sprot/enzyme.html) (which is incorporated herein by reference). For example, oxidoreductases are classified as oxidoreductases acting on the CH-OH group of donors with NAD⁺ or NADP⁺ as an acceptor (EC 1.1.1); oxidoreductases acting on the aldehyde or oxo group of donors with NAD⁺ or NADP⁺ as an acceptor (EC 1.2.1); oxidoreductases acting on the CH-CH group of donors with NAD⁺ or NADP⁺ as an acceptor (EC 1.3.1); oxidoreductases acting on the CH-NH₂ group of donors with NAD⁺ or NADP⁺ as an acceptor (EC 1.4.1); oxidoreductases acting on the CH-NH group of donors with NAD⁺ or NADP⁺ as an acceptor (EC 1.5.1); oxidoreductases acting on NADH or NADPH (EC 1.6); and oxidoreductases acting on NADH or NADPH with NAD⁺ or NADP⁺ as an acceptor (EC 1.6.1).

On page 19, please delete the paragraph on page 19, line 25, to page 20, line 10, and substitute therefor:

B2

Methods for determining that two receptors are in the same family are well known in the art. For example, one method for determining if two receptors are related is BLAST, Basic Local Alignment Search Tool, available on the National Center for Biotechnology Information web page (www.ncbi.nlm.gov/BLAST/) (which is incorporated herein by reference). BLAST is a set of similarity search programs designed to examine all available sequence databases and can function to search for similarities in protein or nucleotide sequences. A BLAST search provides search scores that have a

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well-defined statistical interpretation. Furthermore, BLAST uses a heuristic algorithm that seeks local alignments and is therefore able to detect relationships among sequences which share only isolated regions of similarity (Altschul et al., J. Mol. Biol. 215:403-410 (1990), which is incorporated herein by reference).

On page 20, please delete the paragraph on page 20, line 27, to page ~~21~~, line 16, and substitute therefor:

B3

A second resource for identifying members of a receptor family is PROSITE, available at ExPASy (www.expasy.ch/sprot/prosite.html) (which is incorporated herein by reference). PROSITE is a method of determining the function of uncharacterized proteins translated from genomic or cDNA sequences (Bairoch et al., Nucleic Acids Res. 25:217-221 (1997), which is which is incorporated herein by reference). PROSITE consists of a database of biologically significant sites and patterns that can be used to identify which known family of proteins, if any, the new sequence belongs. In some cases, the sequence of an unknown protein is too distantly related to any protein of known structure to detect its resemblance by overall sequence alignment. However, related proteins can be identified by the occurrence in its sequence of a particular cluster of amino acid residues, which can be called a pattern, motif, signature or fingerprint. PROSITE uses a computer algorithm to search for motifs that identify proteins as family members. PROSITE also maintains a compilation of previously identified

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33
Cort motifs, which can be used to determine if a newly identified protein is a member of a known protein family.

On page 21, please delete the paragraph on lines 17-25 and substitute therefor:

34
A third resource for identifying members of a receptor family is Structural Classification of Proteins (SCOP) available at SCOP (scop.mrc-lmb.cam.ac.uk/scop/) (which is incorporated herein by reference). Similar to PROSITE, SCOP maintains a compilation of previously determined protein motifs for comparison and determination of related proteins (Murzin et al., J. Mol. Biol. 247:536-540 (1995), which is incorporated herein by reference).

On page 22, after "SEARCHABLE MOTIF AND PATTERN DATABASES" and "WEBSITES" on lines 3-4, please delete lines 5-11 and substitute therefor:

PROSITE expasy.hcuge.ch/sprot/prosite.html

BLOCKS www.blocks.fhcrc.org/blocks_search.html

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PRINTS www.biochem.ucl.ac.uk/bsm/dbbrowser/PRINTS/PRINTS.html

PIMA dot.imgen.bcm.tmc.edu:9331/seq-search/protein-search.html

PRODOM protein.toulouse.inra.fr/prodom.html

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On page 22, after "MOTIF AND PROFILE SEARCHES" and "WEBSITES" on line 12, please delete lines 13-22 and substitute therefor:

REGULAR EXPRESSION SEARCH

www.ibc.wustl.edu/fpat/

PROFILESEARCH

www.seqnet.dl.ac.uk/hhg/PROFILESE.html

B6 PATSCAN WWW-

c.mcs.anl.gov/home/overbeek/PatScan/HTML/patscan.html

PATTERNFIND

ulrec3.unil.ch/software/PATFND-mailform.html

PROFILE

lenti.med.umn.edu/MolBio_man/chp-10.html#HDR1

On page 23, please delete lines 1-2 and substitute therefor:

B7 PMOTIF

alces.med.umn.edu/pmotif.html

HMMER

genome.wustl.edu/eddy/HMMER/

On page 23, after "WWW AND FTP SERVERS FOR SINGLE SEQUENCE EXHAUSTIVE DATABASE SEARCHES" and "WEBSITES" on lines 3-5, please delete lines 6-8 and substitute therefor:

B8 BLAST

www.ncbi.nlm.nih.gov/BLAST/

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cont
BLITZ

www.ebi.ac.uk/searches/blitz_input.html

FASTA

www.genome.ad.jp/ideas/fasta/fasta_genes.html

On page 23, after "FTP ADDRESSES FOR MOTIF AND PROFILE
SEARCH PROGRAMS" and "WEBSITES" on lines 9-10, please delete
lines 11-17 and substitute therefor:

BARTON'S FLEXIBLE PATTERNS

geoff.biop.ox.ac.uk/

PROPAT

ftp.mdc-berlin.de/

SOM

ftp.mdc-berlin.de/pub/neural

BG
SEARCHWISE

sable.ox.ac.uk/pub/users

PROFILE

ftp.ebi.ac.uk/pub/software/unix/

TPROFILESEARCH

ftp.ebi.ac.uk/pub/software/vax/egcg

CAP

ncbi.nlm.nih.gov/pub/koonin/cap

⤵ Please amend the claims as follows ⤵

Please cancel ~~claim~~ claim 10.

B10 Sub D1
9. (Amended) A method for identifying a population of
bi-ligands to receptors in a receptor family, comprising